



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/527,352	03/17/2000	Edward L. LeCluyse	421/17/2	3016

25297 7590 07/12/2002

JENKINS & WILSON, PA  
3100 TOWER BLVD  
SUITE 1400  
DURHAM, NC 27707

EXAMINER

AFREMOVA, VERA

ART UNIT PAPER NUMBER

1651

DATE MAILED: 07/12/2002

15

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**Application No.  
**09/527,352**Applicant(s)  
**LeCruse et al.**Examiner  
**Vera Afremova**Art Unit  
**1651**

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED May 31, 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on May 31, 2002. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see NOTE below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE:

3. ☐ Applicant's reply has overcome the following rejection(s):

4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
see attached

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: none

Claim(s) objected to: none

Claim(s) rejected: 25-38

Claim(s) withdrawn from consideration: \_\_\_\_\_

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_

10. ☐ Other: \_\_\_\_\_

Art Unit: 1651

**Attachment to Advisory Action**

***Response to Arguments***

Applicant's arguments filed 5/31/2002 have been fully considered and are not persuasive for the reasons below. The amendment to the claims 25-38 does not overcome the rejection of record under 35 U.S.C. 102(b) as being anticipated by LeCluyse et al. [U] or Liu et al [IDS-EE] and under 35 U.S.C. 103(a) as being unpatentable over LeCluyse et al. [U] or/and Liu et al [IDS-EE] taken US 5,602,026 [A], Liu et al. [IDS-DD] and Poole et al. [U].

With regard to the reference by LeCluyse et al. [U] applicants argue (response pages 5-6) that the method of the cited reference is drawn to monitoring of a single compound or to monitoring of a "marker" compound (fluorescent dye). Applicants argue that there is no indication that the multiple compounds comprising both "marker" and "candidate" compounds are employed in the method of the cited reference. However, neither the pending claims nor the instant as-filed specification provide specific definitions for the "candidate" compound. The office broadly interprets the "candidate" compound as any compound which is present in the hepatocyte culture system of LeCluyse et al., for example: buffer or DMEM ingredients. Applicants also argue that the method of the cited reference by LeCluyse et al. does not recite step of detecting an amount of a marker compound. This is not found convincing because the cited reference recites monitoring of marker compound with the fluorescent microscopy. One who is monitoring fluorescent marker compound can clearly see the differences in the intensity

Art Unit: 1651

of fluorescent marker. The relative amount of marker compound is all what is required by the presently claimed method.

With regard to the reference by Liu et al [IDS-EE] applicants argue (response pages 6-7) that the method of the cited reference is uncertain whether the model compounds including "marker" and "candidate" compounds are provided together or separately. Yet, the method of claim 25 requires "simultaneously" exposing both compounds to the hepatocyte culture rather than exposing both compounds together in the same culture. Moreover, the cited reference recites a comparative analysis of several model compounds and it teaches the differences in biliary excretion for at least 4 groups of various model compounds including marker and candidate compounds. Applicants' argument that the cited reference does not recite the amount of marker compound indicating the susceptibility of the candidate compound to the biliary excretion (BE) is not persuasive because the cited reference teaches that the disclosed system is useful "to investigate drug-drug interactions relevant to BE" (see last two lines). Therefore, the reference is considered to teach and/or to suggest a competition assay as it is intended for the presently claimed method.

The secondary references US 5,602,026 [A], Liu et al. [IDS-DD] and Poole et al. [U] are relied upon for the disclosure drawn to the use of various hepatocyte cells and cultures for monitoring model compounds in the *in vitro* and in the *in vivo* systems.

Art Unit: 1651

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (703) 308-9351. The examiner can normally be reached on Monday to Friday from 9:00 to 5:30.

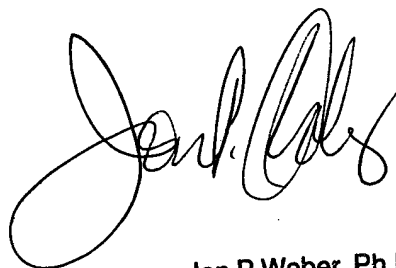
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vera Afremova,

Art Unit 1651

July 10, 2002.

A handwritten signature in black ink, appearing to read 'Jon P. Weber', with a large, stylized loop at the end.

Jon P. Weber, Ph.D.  
Primary Examiner